

# AUTONOMOUS VERSUS REFLEXOGENOUS ACTIVITY OF THE CENTRAL NERVOUS SYSTEM<sup>1</sup>

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## ABSTRACT

Experiments are reported which have produced conclusive evidence in favor of autonomous, as against reflexogenous, origin of central nervous function. Both the drive (automatism) and the pattern (coordination) of central activity are fundamentally intrinsic properties of the centers.

1. Differentiated spinal cord of amphibian larvæ was transplanted under the back skin and connected with a transplanted limb as motor effector. Such "deplanted" isolated centers, while undergoing structural disorganization, exhibit recurrent seizures of rhythmic spontaneous activity for many months. Most parts of the nervous system seem to possess rhythmic automaticity, although this remains largely latent so long as the part is connected with, and subordinated to, other centers. Reflex activity appears in the deplanted centers only secondarily, after the endogenous activity has been going on for some time.

2. The fact that the central discharge patterns of coordination, as they self-differentiate, are laid down in terms of sequences of individual muscle contractions with no regard to the effectiveness or ineffectiveness of the contractions for the animal as a whole, is proved by the development of reversed locomotion in animals of which the legs have been reversed in the prefunctional stage. No adjustments are ever observed in amphibians.

3. The fact that the basic self-differentiated patterns of coordination are unmodifiable even in mammals, is proved by the permanently reversed functioning of the legs of rats after tendon crossing (Sperry).

In conclusion, the basic patterns of coordination are centrally preformed, do not arise by trial and error, and cannot be remodeled by experience.

THE useful operation of a machine depends on two factors, energy supply and a proper structural design to transform and distribute the energy appropriately. The operation of our nervous system likewise depends on two factors, generation of nervous activity, and a pattern for the selective distribution of that activity. Without proper devices for coordinated distribution, excitation produces mere convulsions. Conversely, without driving force the most appropriately designed nervous mechanism remains an idling plant. Consequently, when speaking of the origin of

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nervous activity, we must split the problem into one of the drive and one of the pattern of action.

These are not necessarily of joint origin. The drive may come from without—be *exogenous* to the nervous system,—or from within, being *automatic*. Impulses, whether generated in one way or the other, are then distributed according to patterns which may be *inherited*, that is, devised by autonomous laws of the developing nervous system, or individually *acquired*, that is, molded by extraneous influences, through practice and experience. External incentive versus automatism, stimulus-determined versus autonomous response,—these are the perpetual issues facing the student of behavior. To decide among them, is an empirical problem and not one of logic. Therefore, we shall not enter into the academic discussion which has been carried on about the subject by physiologists, psychologists, educators, and even sociologists, but merely present some of the modest earth-bound efforts of the experimental biologist to provide those discussions with a more solid foundation of facts.

First, let us consider the *drive* of the nervous system. For a long time physiologists have been partial to the thesis that it is basically exogenous rather than automatic, reflexogenous rather than spontaneous. The organism was represented as a reflex machine with input, transformer, and output, and all nervous activity was thought to arise from a sensory stimulus or a chemical stimulant carried in the blood. The first serious breach in the pure reflex theory came with the discovery that the respiratory center continues to discharge rhythmic bursts of impulses even when completely isolated. Spontaneous discharges of this order were obtained by *Adrian* and coworkers (*Adrian* 1932) and by *Bronk* and *Ferguson* (1935) from the respiratory center of vertebrates, and by *Adrian* and by *Prosser* (1936) from the ganglia of some arthropods. Lately, the periodical fluctuations of electrical potential in the brain cortex, so-called brain waves, have been advanced as evidence of the spontaneous activity of this highest nerve center.<sup>3</sup> Yet, these cases could still be considered as exceptions rather than the rule, so long as all other nerve tissue could be thought of as devoid of spontaneous activity.

<sup>3</sup> The fact that the amphibian embryo displays motor activities before the sensory system is developed (*Coghill* 1929) furnishes a strong argument in favor of central automatism; however, occasional doubts have been raised regarding the conclusiveness of this argument on the grounds that the possibility of irritation of the centers by substances carried in the blood or other body fluids was not excluded.

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However, this thought can no longer be maintained in the light of the experiments which I am about to report, and which have shown that the capacity for spontaneous, rhythmic, activity is indigenous to most central nervous substance, although it takes special measures to bring it out. These measures consist of allowing the centers to undergo some degree of destruction and degradation. This is achieved by a method which we may call "deplantation."<sup>4</sup> Excised fragments of central nervous system are embedded in a well-vascularized, but otherwise indifferent, tissue. The gelatinous connective tissue of the dorsal fin of amphibians is excellently suited for this purpose (Fig. 1). A bit

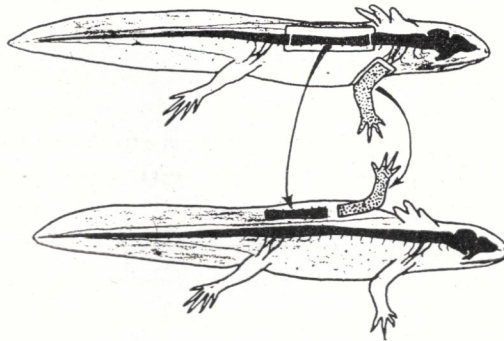


FIG. 1. Deplantation of a fragment of spinal cord (black) and transplantation of a limb (stippled) to the dorsal fin of a salamander larva. Within a few weeks nerves from the deplant grow into the limb effecting functional connections with its muscles and skin.

of brain or spinal cord deplanted into this tissue suffers serious disorganization and loses part of its cell content by degeneration. The remaining part, however, survives and becomes functional. To assay its activities, we provide the deplanted center with the most natural and adequate detector, namely, a group of muscles: We transplant a limb into its vicinity, taking care that nerve connections can be established between the two grafts. Thus, we produce an isolated complex, consisting of a deranged nerve center, a limb, and random nerve connections between them, the whole unit supplied by the common blood stream, but otherwise independent from the host animal (*P. Weiss* 1940).

No sooner have the nerve fibers from the deplanted center

<sup>4</sup> *Przibram* (1930) defines "deplantation" as any "insertion of a removed part in a different location." In the more restricted sense in which we propose to use the term, however, it connotes a marked degradation of organization suffered by a part which has been transplanted into an atypical location.

united with the muscles of the limb graft, than the latter begins to register almost incessant *spontaneous activity*. Without any external stimulus, in a perfectly quiescent host body, the grafted center discharges into the limb in intermittent spells which range from continuous arrhythmic fibrillations to strong synchronized pulses of a fairly regular rhythm of from 20 to 90 per minute. Frequently a seizure begins with weak irregular twitches and gradually builds up in strength to violent and more synchronized activity during which the limb muscles beat in unison at fairly regular intervals. The seizures come and go for weeks, continuing uninterrupted for hours, and the whole phenomenon has been seen to last for as much as 5 months, which was as long as the animals were kept. The fact that the observed activity really originated within the deplanted centers, was, of course, established beyond doubt by a variety of checks.

*Reflex* responses to touch also appear, but not until many weeks after the onset of spontaneous activity. Hence, the preceding pulsating activity is definitely of automatic and not of reflex origin. It has been obtained thus far from the following variety of grafts (*P. Weiss* 1941): spinal cord from any region and of any length; medulla oblongata; spinal cord slashed or minced and then implanted as a single lump; spinal cord from larvæ as well as from adults; fragments from purely ventral or purely dorsal sectors of the spinal cord, which is particularly remarkable in view of the fact that the dorsal half contains no motor cells, and the ventral half no sensory elements.

The constancy of the phenomenon under such a variety of conditions intimates that we are dealing with a fundamental capacity of all nerve substance which is manifested as soon as the more specialized superstructure of anatomical and functional relations, present in the normal developed nervous system, has broken down. The close connection between derangement and the emergence of automatic seizures can be directly demonstrated (*P. Weiss* 1941). If a spinal limb center and the corresponding limb are deplanted together under careful preservation of their nerve connections (Fig. 2), orderly reflexes are obtained immediately after the operation and during the following days. Gradually, however, the reflex responses become cruder, protracted, and generally disorganized. Significantly, *pari passu* with this deterioration, spontaneous activity makes its appearance.

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Supported by histological evidence, we may consider our deplants as neurone pools in which the typical organization has given way to a random make-up. Such a random neurone pool, however, exhibits many of the functional properties of centers which we have been used to attribute to a definite and minutely arranged neurone architecture. Its discharges are rhythmic, and the participating elements tend to become synchronized with increasing intensity of the reaction. A certain analogy to the heart beat is obvious, and one wonders whether a pacemaker mechanism or some mutual induction among the elements is responsible for the synchronization; but this is for the future to

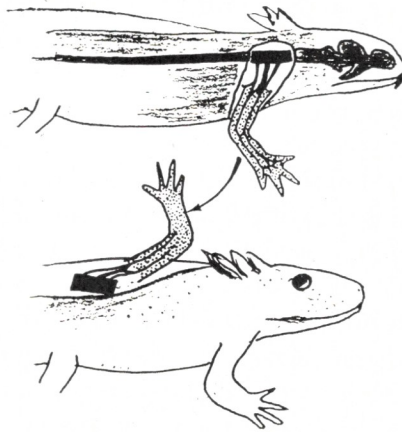


FIG. 2. Deplantation of limb segments of spinal cord with nerves and innervated limb remaining attached.

decide. We are left with the impression that something is constantly being built up in the centers which, upon reaching a certain threshold value, gives rise to a discharge, whereupon a new cycle begins. Again, whether that something consists of an electrostatic field, or metabolites, or something else, only the future will tell with certainty. Our preparations lend themselves readily to a further investigation of these problems.

The reflexes obtained from our neurone pools show some typical attributes of normal reflex action, namely, graded response, spatial summation, temporal summation, and fatigue. In addition to releasing motor responses, afferent impulses also seem to lower the excitability of the whole pool, which often results in a burst of spontaneous activity trailing the reflex.

In view of the random character of our pools, their functional properties will have to be explained on purely statistical assumptions. If we assume that the thresholds of the cell population are distributed according to mere chance, the numbers of cells in each threshold class, plotted against thresholds, would form a normal distribution curve (Fig. 3). Since an afferent input of given

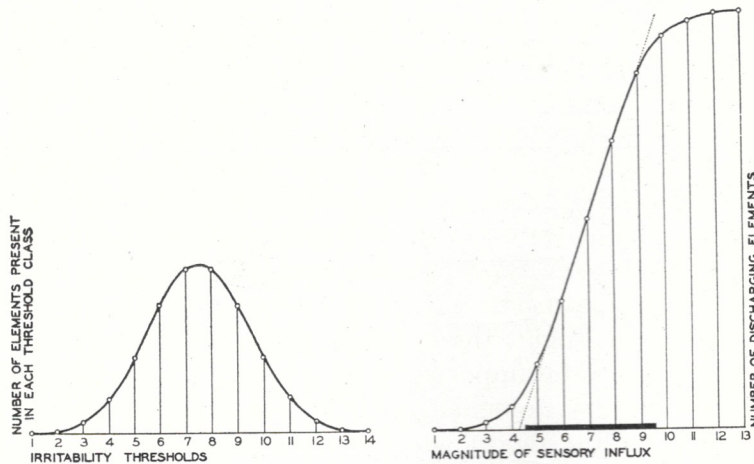


FIG. 3. Normal distribution of the units of a neurone pool according to threshold classes, on the assumption that constitutional threshold variations are of random character.

FIG. 4. Area enclosed by the curve of Fig. 3 (in arbitrary units) plotted against the individual threshold values. This curve follows within its middle range (marked by a black bar) a nearly linear course. Since this range includes almost 90 per cent of all elements present, it follows that every stepping up of the sensory effect, either by increase of the peripheral stimulus or by spatial or temporal summation, produces a corresponding increase in the number of discharging efferent units.

strength will activate all elements of the corresponding and lower thresholds, the number of discharging elements is expressed by the area of the binomial function up to that threshold value. Since the curve representing the integral of the binomial function is in the major part of its course sufficiently close to a straight line (Fig. 4), we realize that in a random pool of neurones there will be some proportionality between sensory input and response.<sup>5</sup> The implications of this thought for the physiology of the normal nervous system are obvious, but have not yet been followed up in detail.

<sup>5</sup> What the observations have thus far established, is only an estimated gross proportionality between stimulus and effect; but whether this proportionality follows a linear or some other function has not been ascertained and will remain unknown until quantitative tests have been applied. We merely intend to show that approximate linearity would bear out the randomness of the neurone distribution in the pool.

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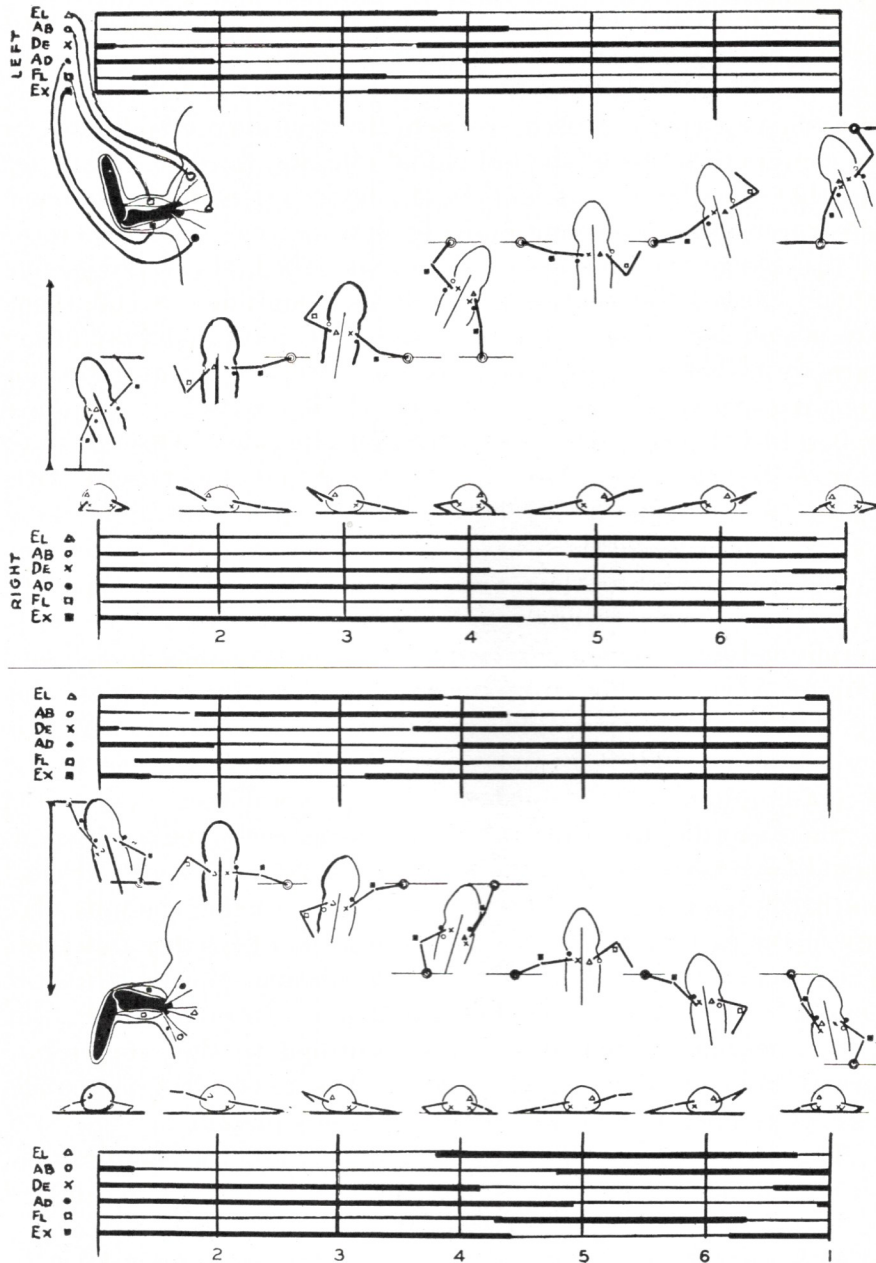


The intensity of spontaneous activity fluctuates with the composition of the blood of the host animal. Changes in the blood produced by light exercise of the body cause a marked increase in the excitability of the deplants, which expresses itself in increased spontaneous activity and lower reflex thresholds. Whether anoxemia, acidity, carbondioxide, or metabolites are involved, has not yet been determined. This sensitizing effect is often sufficient to start a temporarily quiescent deplant off on a spell of activity. Observations like these suggest that the cyclic process underlying the rhythmic spontaneous discharges is actually going on in the neurone pool all the time, whether a discharge appears or not. An effective discharge will result only if the process reaches a critical threshold intensity. Otherwise it merely conditions the nerve cells so that they can go off under such additional stimuli as may come in from other sources, provided the total sum adds up to threshold intensity.

Viewed in this light, the endogenous pulse of a nerve cell becomes of fundamental importance for nervous activity, even when it does not register immediately as a visible motor effect. And instead of regarding spontaneous activity as an exceptional manifestation of cortex, respiratory center, and insect ganglia, we may have to concede it to all nerve substance. Then, of course, the question arises as to what causes it to remain latent in most of the normal centers. We do not know the answer, but our experiments suggest that the repressing effect is somehow tied up with the normal organization of the centers, and disappears with the latter. In this connection we may point to the striking resemblance between the seizures of our deranged deplants and epileptiform seizures in human patients. It will be interesting to examine whether this resemblance is purely superficial or really pertinent.

Let us now turn to the second point of our program—the *patterns* of nervous activity. Are they of central or of extraneous origin? Recent experiments have given an incontrovertible answer. The patterns underlying the basic acts of behavior of an animal are developed by *self-differentiation* within the centers, without experience, and, indeed, sometimes in spite of experience.

Coordinated locomotion requires that the muscles be engaged in a definite chronological order. The correct timing and dosing of the individual contractions is all that distinguishes the harmony



FIGS. 5 AND 6. Diagrams indicating the "scores" of muscle action in the forelimbs during a single step of a walking salamander, as reconstructed from motion pictures.

FIG. 5. Normal animal.

FIG. 6. Experimental animal with reversed forelimbs. Only six main muscle groups are recorded: elevators, abductors, depressors, and adductors of the upper arm;

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of the gait from the discord of a convulsion. The muscles are played by the centers according to a definite "score," like an orchestra (Fig. 5). Now, previous experiments (*P. Weiss* 1936) have shown that the muscle scores for locomotion are laid down in the centers in terms of the individual muscles, muscle for muscle, and that these scores, at least in the lower vertebrates, are fixed and inaccessible to reconditioning by experience. If, for instance, we disarrange the muscles so as to make their play yield incongruous effects, the centers, nevertheless, continue to call them into action according to the old score, as before; and they never learn to do better. The most extreme case is illustrated by the following experiment on salamanders (*P. Weiss* 1937). A limb is replaced by its counterpart from the opposite side. This amounts to reversing the position of the flexor and extensor muscles with regard to the body as a whole (Fig. 6). The central nervous system, however, persists in sending out the impulse pattern in the old order meant for the normal arrangement, and, consequently, such animals with reversed limbs, when bent on forward locomotion, actually move backward, and when intending to retreat, actually advance (Fig. 6). In spite of their predicament, the animals have never been able to adjust their coordination to the new situation. There is no trace of reeducation, and the scores of coordination, once established, prove unmodifiable.

Since coordination cannot be relearnt, it seems unlikely that it should have been learnt in the first place. Nevertheless, a crucial test had to be made, and this was done by reversing the musculature in the early larval stage, before there had been any function. When such animals later take up ambulation, the limbs again move in reverse, and do so throughout life. In other words, the central nervous system discharges according to the score for a normal unreversed limb, although it has never had a chance actually to operate a normal limb, as none is present.

This is definite proof that the basic patterns of coordination self-differentiate within the central nervous system. They differ-

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flexors and extensors of the fore-arm. The position of these muscles is indicated in the inset. The record for the left limb is on top and that for the right limb at the bottom of each diagram. In the center seven phases of the actual movement of the animal are presented in dorsal and rear views; the points in which the hand is put down on the ground, and which serve as pivotal points for the body during the subsequent phase of movement, are marked by circles.—The "scores" are identical for the normal (Fig. 5) and reversed (Fig. 6) limbs, but, in the latter case, result in a backing movement.

entiate into what would be the correct score for a normal limb, regardless of whether or not the movements which they produce will actually be of service to the animal. This does not preclude learning by experience in lower vertebrates altogether. It merely specifies that the learning process must avail itself of the basic preformed patterns of performance; learning may be able to facilitate, suppress, dissociate or rearrange combinations of *existing* patterns, but it cannot break the individual patterns down and reconstruct or remodel them to suit emergency situations.

In view of these results on lower vertebrates, a re-investigation of the situation in higher mammals became imperative; for "natura non facit saltum." A student of mine, Mr. Sperry, was charged with exploring in the rat the effects which crossing of the tendons of antagonistic foot muscles would have on locomotion (Sperry 1940). Each muscle pulling on the wrong side of the skeleton (Fig. 7), at first, of course, produced effects, which were the reverse

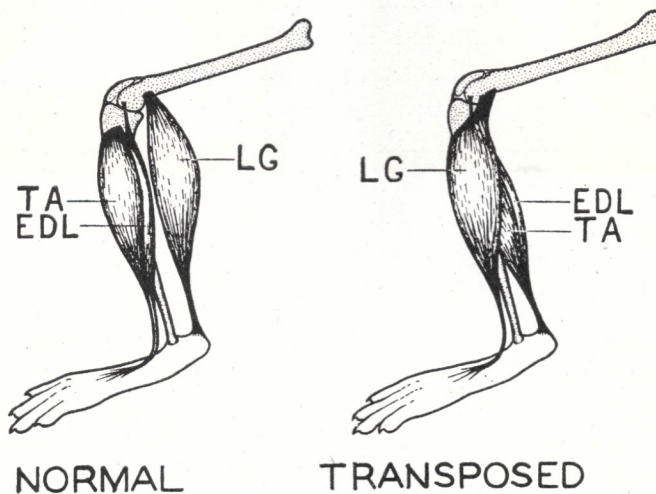


FIG. 7. Transposition of the tendons of the leg muscles in the rat so as to reverse the mechanical action of these muscles (after Sperry). *TA*, anterior tibial muscle; *EDL*, long extensor of the digits; *LG*, lateral gastrocnemius. (All other muscles removed.)

from what the animal intended. But according to the literature a gradual recovery of normal function should have been expected. No such readjustment, however, occurred even under most crucial training conditions, the muscles maintaining their reversed play (Fig. 8) throughout life. Basic coordination patterns are as fixed in the rat as they are in amphibians, and experience can have had

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no part in their establishment. The same is presumably true of higher mammals.

But how about man? Do we not know from innumerable experiences of surgeons that a patient whose paralyzed muscles have been substituted by healthy muscles of different function, gradually learns to put the new combination of muscles to good use in walking and other performances? Jointly with our Orthopedics Department, we are conducting at present a thorough re-investigation of this whole problem. But even on the basis of our present knowledge, it seems safe to predict, that whenever a patient learns to use a muscle in a different sequence than that provided for in the inherited pattern of gait, this learning act is on



FIG. 8. Foot action in the extension phase of a movement. (After Sperry.) (a) Rat the tendons of which were severed and resutured without crossing; plantar flexion of foot. (b) Rat with crossed tendons; reversal of foot movement, *i.e.*, dorsal flexion.

the same level as the learning of trick movements or other skills; in other words, it is a *new* performance, not a remodeled old one. Voluntary effort of the cortex can do these things which lower vertebrates cannot do. While even conscious effort cannot recondition the basic inherited patterns of coordination, it can learn to supersede them by novel ones, which will last so long as the cortex acts, obscuring, but not abolishing, the lower autonomous patterns. Apparently, mammals have acquired the ability to engage muscles in arbitrary combinations only during fairly recent stages of their evolutionary course. This fact is significantly reflected in the increasing prominence which the pyramidal (cortico-spinal) system has gained in higher mammals: through this tract the cortex can activate spinal motor neurones directly by a short cut around the hierarchy of subcortical mechanisms which operate the inherited patterns.

Coordination *by experience*, therefore, is a secondary, and highly specialized, affair. All primary coordination exists *by pre-design*, established in the pre-functional phase of neurogenesis, independent of, and unresponsive to, experience.

In summarizing, we recognize that the nervous system, far from playing the passive role which at times has been attributed to it, provides part of its drive and part of its patterns of action from its own inherited resources. *Automatism*, though manifesting itself under normal conditions only in certain kinds of centers (respiratory center, arthropod ganglia), may yet exist in all centers as a conditioning mechanism, disposing for discharge, rather than actually discharging, central neurones. And *autonomy* must be conceded at least to the basic patterns of performance of all animals from the lowest to the highest.

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